# Surgical, Pharmacological, and Technological Advances in Adult and Pediatric Urology – State of the Art

Highlights of the 7th Annual NYU Department of Urology Postgraduate Course December 7-9, 2000, New York, NY

[*Rev Urol.* 2002;4(1):24–33]

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Key words: Voiding dysfunction • Stress incontinence • Sling procedure • Refractory detrusor instability • Overactive bladder • Renal imaging • MRI • Prostate cancer • Sexual dysfunction

he Department of Urology of New York University (NYU) School of Medicine hosted its 7th Annual Postgraduate Course December 7 to 9, 2000, entitled "The Surgical, Pharmacological and Technological Advances in Adult and Pediatric Urology - State of the Art." The course was attended by urologists representing 32 states and 12 countries. The program focused on voiding dysfunction and female urology, erectile dysfunction, renal imaging, prostate cancer, BPH, bladder, and bladder cancer. It is not feasible to present in a single meeting summary all of the clinically important

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information presented at this 21/2-day meeting. This review will highlight the information felt to be of greatest interest to the practicing urologist.

# Voiding Dysfunction and Female Urology

The session on voiding dysfunction was chaired by Dr. Victor Nitti, Associate Professor and Vice Chairman of Urology at NYU School of Medicine. The invited faculty included Alan Wein (University of Pennsylvania), Jerry Blaivas (Cornell Medical School), and Sender Herschorn (University of Toronto).

Classification of Voiding Dysfunction Dr. Wein reviewed the different classification systems for voiding dysfunction. The functional classification of voiding dysfunction describes the dysfunction in terms of whether the deficit produced effects on filling/storage or emptying/voiding. A storage failure results because of bladder or outlet abnormalities or a combination of both. The bladder abnormalities include involuntary bladder contractions, low compliance, and hypersensitivity. The outlet abnormality in failure to store is decreased outlet resistance. Emptying failure likewise can occur because of bladder or outlet abnormalities or both. The bladder abnormalities include inadequate or unsustained bladder contractility, and the outlet abnormalities include anatomic obstruction or sphincter dyssynergia.

Dr. Wein emphasized that some patients do not only have a discrete storage or emptying failure, and the possible existence of a combination of deficits must be recognized to properly utilize the classification system.

# Pharmacotherapy of Voiding Dysfunction

Dr. Wein presented an overview of drug therapy for filling and storage disorders. There has been a great deal of interest in the development of better drugs to inhibit bladder contractility. Dr. Wein indicated that the First International Consultation on Urinary Incontinence recommended propantholene, tolterodine, oxybutynin, imipramine, and desmopressin as effective drugs for the treatment of bladder overactivity. Anticholinergic agents have been known to increase the volume of the first involuntary bladder contraction, decrease the

sant activity. Bladder contraction is mediated primarily by the M3 receptor. Unfortunately, the M3 receptor is also responsible for salivary secretion and intestinal contraction. Therefore, M3-selective agents are unlikely to eliminate adverse events associated with the anticholinergic agents.

The tricyclic antidepressants facilitate urine storage primarily by decreasing bladder contractility, and to a much lesser degree by increasing outlet resistance. Imipramine has prominent systemic anticholinergic effects, but only a weak antimuscarinic effect on the bladder smooth muscle. Therefore, it is reasonable to combine imipramine with a pure anticholinergic agent.

To decrease side effects, drugs altering bladder contractility have been administered intravesically. The symptomatology and often requires anesthesia for administration. The advantage of this intervention is that the positive clinical effects last up to 6 months. Resiniferatoxin is a drug similar to capsaicin, except that it is 1,000 times more potent in producing desensitization and less potent at producing inflammation.

# Pathophysiology of Stress Incontinence

Dr. Blaivas presented a lecture on the pathophysiology of stress urinary incontinence. From a physiologic standpoint, Dr. Blaivas indicated there are two components to sphincteric incontinence: intrinsic sphincter deficiency and urethral hypermobility. Intrinsic sphincter deficiency connotes a weakness of the sphincter mechanism itself. Urethral hypermobility denotes a support defect of the urethra and vesical neck during increase of abdominal pressure.

Intrinsic sphincter deficiency can be caused by anything that impairs the active forces (neuropathy involving the pelvic nerve from childbirth or other insults), or anything that impairs the active forces (scarring from previous surgery or infection). Urethral hypermobility is caused by conditions that weaken pelvic support structure, such as childbirth injury and pelvic surgery. According to Dr. Blaivas, the leak-point pressure is the best measure of sphincteric strength. The lower the leak-point pressure, the weaker the sphincter. The sphincter may be "weak" because of loss of its active and/or passive properties, or because the walls of the urethra are pulled open, widened, and shortened by a traction phenomena when there is prolapse of other origins.

Desmopressin lacks significant

Surgical Treatment of Stress Incontinence

Dr. Blaivas also discussed the surgical treatment of stress incontinence. He

The primary disadvantage of anticholinergic agents is that the muscargenic cholinergic receptors are ubiquitous and, therefore, they cause troublesome side effects, such as dry mouth, blurred vision, and constipation.

amplitude of involuntary bladder contraction, and increase total bladder capacity. Unfortunately, the "warning" time is not effected. It is for this reason that anticholinergic therapy is often combined with behavioral intervention. The primary disadvantage of anticholinergic agents is that the muscarinic cholinergic receptors are ubiquitous and, therefore, they cause troublesome side effects, such as dry mouth, blurred vision, and constipation. Somnolence and cognitive dysfunction can also be a problem, especially in the elderly. Dr. Wein estimated that up to 50% of individuals discontinue anticholinergic therapy because of adverse events. Antidepressants such as imipramine have systemic anticholinergic side effects and hosts of other potential side effects related to its antidepresonly disadvantage is that the drug has to be administered via a catheter. Some small studies suggest intravesical administration has an advantage related to adverse effects.

effects on bladder smooth muscle; however, it does elicit a pronounced antidiuretic effect. Thus, it can be used for the treatment of nocturia in those individuals without predisposition to congestive failure.

One attractive new modality for the treatment of overactive bladder and bladder hypersensitivity is to depress sensory neurotransmission. Capsaicin causes desensitization of C-fiber sensory afferent nerves by initially releasing and emptying the stores of neuropeptides that serve as sensory neurotransmitters. Capsaicin does, however, cause intense local

indicated that there are over 150 operations for the treatment of stress incontinence. These surgical procedures can be categorized into four groups: retropubic suspension, transvaginal suspension, pubovaginal slings, and anterior colporraphy.

The overall success rate of anterior colporraphy as an isolated procedure is generally agreed to be poor. The Burch colposuspension and fascialpubovaginal sling, according to

procedures to reduce morbidity and operative time. Alternative sling materials include allografts, xenografts, and synthetics. Alternative sling techniques include bone anchors, patch slings, transvaginal slings, and tension-free vaginal tape (TVT).

There has been a great deal of interest in utilizing cadaveric fascia. In Dr. Nitti's opinion, this option reduces operative and recovery times; however he expressed a con-

There has been a great deal of interest in utilizing cadaveric fascia.

Dr. Blaivas, are the "gold standards" against which to compare other operations. The long-term cure rate for the Burch procedure is approximately 80%. The success rate of the fascialpubovaginal sling is equivalent.

The new operations attempt to rival the Burch and the pubovaginal sling procedures by accomplishing the same goals with less morbidity, ie, smaller incision, less resection, less blood loss, less urinary retention, and less detrusor overactivity. It is unclear whether these new procedures in fact achieve these objectives.

Dr. Nitti discussed modifications of the sling procedure for the treatment of stress incontinence. According to the American Urological Association Female Stress Urinary Incontinence Clinical Guidelines, sling procedures and retropubic suspensions have the best long-term cure rates for stress incontinence. The primary advantage of slings is that they correct both support defects and intrinsic sphincter dysfunction. Retropubic suspensions and slings are the most efficacious procedures for long-term success; however, they have slightly greater complication rates, incidence of postoperative voiding dysfunction, and longer convalescence. There have been many recent attempts to modify sling

cern regarding the lack of long-term data, because histological studies suggest there may be issues related to durability.

One of the advantages of the transvaginal bone-anchored sling is that the procedure is done completely transvaginally. The bone anchors enter the pubic bone. Another option is TVT. This approach can also be done transvaginally. The limitations of both the bone anchor and TVT are the increased cost and lack of long-term efficacy data. According to Dr. Nitti, patients should be counseled about the advantages and disadvantages of all

overactive bladder. He defined overactive bladder as representing symptoms of frequency, urgency, and urge incontinence and detrusor instability as urodynamically proven involuntary detrusor contractions in the absence of neurological disease. Refractory detrusor instability implies the failure of behavioral modification, pharmacotherapy, or physiotherapy. The goal of intervention in these individuals is to relieve or reduce the symptoms and improve bladder function. Dr. Nitti emphasized that all of these individuals must undergo a comprehensive evaluation that includes postvoid residual, comprehensive urodynamic testing, cystoscopy, and urine cytology. If there is any suspicion of neurologic disease based on history, a comprehensive neurologic evaluation should also be performed. This is especially true in younger individuals. The therapeutic options include secondary pharmacotherapy, augmentation cystoplasty, and neuromodulation. Secondary pharmacology includes the combination of anticholinergic and tricyclic agents. There have been preliminary studies demonstrating the efficacy of intravesical installation of resiniferatoxin. Bladder augmentation in many cases will improve

There have been several preliminary studies reporting the success of neuromodulation for refractory detrusor instability.

the different options. Decisions essentially come down to a faster procedure with quicker recovery versus the uncertainty of outcome and risk potential of allografts, zenografts, and synthetics. Chronic complications appear to be equivalent.

Management of Refractory Detrusor Instability and Overactive Bladder Dr. Nitti presented a discussion on refractory detrusor instability and bladder storage with excellent results achieved in up to 95% of cases. The primary complications include recurrent urinary tract infection, persistent mucus, stone formation, incomplete emptying requiring catheterization, metabolic disturbances, perforation, and secondary tumor.

There have been several preliminary studies reporting the success of neuromodulation for refractory detrusor instability. The mechanism for efficacy is not totally understood. Stimulation of the sacral nerves via an electrical implant can inhibit inappropriate bladder behavior. Longer-term data indicate that the nerve stimulation has been effective in approximately 50% to 60% of men with refractory urge incontinence. It the ureter, which may be the cause of refractory strictures.

Evaluation of the Indeterminate Renal Mass

Dr. Bosniak delivered a lecture on the evaluation of renal tumors in the indeterminate lesion. Dr. Bosniak

One of the primary advantages of intraluminal ultrasound is the ability to identify the location of peripelvic vessels at the time of endopylotomy.

is important to recognize that the success is limited to those individuals who successfully responded to a percutaneous test stimulation.

Dr. Nitti concluded that there are a variety of treatments available for refractory detrusor instability. In most cases, these treatments require a strong desire on the part of the patient to treat their symptoms and involve some degree of commitment and risk.

#### Renal Imaging

Dr. Taneja, Assistant Professor of Urology at NYU School of Medicine, moderated the session on renal imaging. The faculty included Drs. Michael Grasso (NYU), Gary Israel (NYU), and Morton Bosniak (NYU).

#### Intraluminal Ultrasound

Dr. Grasso presented an update on intraluminal ultrasound. Dr. Grasso has been one of the pioneers in the application of this technology in urology. One of the primary advantages of intraluminal ultrasound is the ability to identify the location of peripelvic vessels at the time of endopylotomy. Dr. Grasso showed several cases in which significant hemorrhage would have been encountered if the intraluminal ultrasound were not used. The intraluminal ultrasound can also aid in the detection of stones impacted in developed the classification of renal cystic lesions that is widely utilized.

Owing to the widespread use of sonography and computed tomography (CT) imaging, a greater number of renal masses are being detected. According to Dr. Bosniak, a critical review of the imaging findings will eliminate the need for unnecessary surgical exploration and nephrectomy.

Not all renal masses that enhance are renal neoplasms, but generally speaking, any renal mass that enhances with intravenous contrast should be considered a renal neoplasm until proven otherwise. Category I masses represents benign cysts. Category II represents mildly complilesion, and these must be removed because of the 50% probability of malignancy. Category IV lesions are cystic but with definite solid elements, indicating malignancy. Abscesses can look like cystic carcinomas. If abscess is considered, needle aspiration should be performed. A hematoma demonstrates high attenuation (50 to 60 H), which does not enhance with contrast. Any lesion that has even a detectable amount of fat represents an angiomyolipoma (hamartoma). On very rare occasions, renal cell carcinomas may contain fat, but these lesions will also contain calcium, a finding not seen with angiomyolipoma. Category II cysts have minimal wall thickening with thin smooth muscle septi. The thinwalled septi may include calcification, but they absolutely do not enhance. High-density renal cysts fit this category. Pseudotumors represent areas of renal hypertrophy and give the appearance of a tumor. The pseudotumors are identical to adjacent renal parenchyma and should not be misdiagnosed as malignancies. Category IIF lesions should be followed carefully. These include high-density cysts greater than 4 cm and cystic lesions

Owing to the widespread use of sonography and computed tomography imaging, a greater number of renal masses are being detected.

cated benign renal cysts, pseudotumors, abscesses, hematomas, infarcts, vascular malformations, localized inflammatory pseudotumors, angiomyolipoma, lymphoma, and metastatic cancer. Category I and Category II masses do not require surgical intervention to rule out primary renal neoplasm. Category III and Category IV cystic lesions require surgical exploration because of the high probability of malignancy. Category III represents the true indeterminate

that have a little more thickening of the walls and a little more irregularity, or proteinacous debris within. Category IIF cysts do not have internal enhancement.

A magnetic resonance imaging (MRI) scan may be useful when the CT scans are not definitive or in the individual with renal insufficiency. The superior contrast resolution of MRI over CT has been most helpful, particularly in small lesions where the reliability of CT numbers due to beam hardening artifacts and other factors have degraded the value of CT.

MRI in the Evaluation of Renal Masses Dr. Gary Israel discussed the evolution of MRI in the evaluation of renal masses and the relative value of MRI and CT in characterizing renal masses. The primary advantages of CT include a shorter imaging time, detection of enhancement by utilizing Housfield units, and the ability to detect calcium. The advantages of MRI include better intrinsic soft tissue contrast, primary multiplanar capability, lack of radiation exposure, and the flexibility to administer gadolinium to patients with renal failure and allergies to iodinated contrast material. A combination of T1-weighted images with and without fat saturation and T2weighted images should be obtained

prior to gadolinium administration. Enhancement may be demonstrated by qualitatively comparing images prior to and after gadolinium or by using subtraction techniques.

Renal cysts demonstrate a uniform hyperintense signal on T2-weighted sequences and may have variable signal intensity on T1-weighted sequences secondary to their content, and there is no enhancement after gadolinium administration.

Renal cell carcinomas demonstrate variable signal intensity in T1weighted and T2-weighted images. Following administration of gadolinium, the first acquisition occurs during the arterial phase and produces a corticomedullary nephrogram. This acquisition is also useful in identifying hypervascular tumors as well as pseudotumors. The second acquisition occurs during the tubular nephrographic phase of enhancement and is useful in identifying enhancing renal masses.

An angiomyolipoma is suggested by a hyperintense signal on T1-weighted images. A hemorrhagic cyst may also have similar signal characteristics. Therefore, it is imperative to compare the non-fat-suppressed T1-weighted images to T1-weighted images performed with selective fat suppression.

Three-Dimensional, Cross-Sectional *Imaging of the Kidney* 

Dr. Taneja discussed three-dimensional (3-D), cross-sectional imaging for the preoperative planning of renal surgery.

The clinical utility of 3-D, cross-sectional imaging parallels the widespread acceptance of partial nephrectomy for

#### **Main Points**

- The First International Consultation on Urinary Incontinence recommends propantholene, tolterodine, oxybutynin, imipramine, and desmopressin as effective drugs for the treatment of bladder overactivity.
- One attractive new modality for the treatment of overactive bladder and bladder hypersensitivity is to depress sensory neurotransmission; capsaicin and resiniferatoxin are two agents that have this effect.
- There are over 150 operations for the treatment of stress incontinence; the Burch colposuspension and fascialpubovaginal sling, according to one expert, are the "gold standards" against which to compare other operations.
- Patients with refractory detrusor instability should undergo a comprehensive evaluation that includes postvoid residual, comprehensive urodynamic testing, cystoscopy, and urine cytology.
- Any renal mass that enhances with intravenous contrast should be considered a renal neoplasm until proven otherwise.
- Category III and Category IV cystic lesions require surgical exploration because of the high probability of malignancy.
- Advantages of MRI for renal imaging include better intrinsic soft tissue contrast, primary multiplanar capability, lack of radiation exposure, and the flexibility to administer gadolinium to patients with renal failure and allergies to iodinated contrast material.
- Three-dimensional MRI is being used to select patients for partial nephrectomy. An advantage of the 3-D MRI is the ability to detect lesions up to .6 mm in size; also, because the 3-D MRI incorporates an MR angiographic phase, the relationship of the vessels to the tumor can be defined.
- A prospective screening study is presently underway that will define the clinical utility of complex PSA as a means to improve the assay's specificity.
- In one expert's opinion, modern prostate brachytherapy is a minimally invasive procedure that offers a viable alternative to surgery and conventional external beam radiation with excellent reported results for the treatment of clinically localized prostate cancer.
- For those surgeons who feel it is prudent to decrease the risk of allogeneic blood exposure in radical prostatectomy, erythropoietin should represent the preoperative blood management strategy of choice.
- Replacement of the hormone dihydroepiandrosterone in postmenopausal women with adrenal lyase deficiency seems to be beneficial in re-establishment of both libido and sexual function.

relatively small renal masses. At NYU, 3-D, volume-rendered MRI is used to evaluate the inter-renal position of the tumor as well as the stage, multifocality, and extrarenal vascular relationships to the tumor.

Dr. Taneja recommends a partial nephrectomy for most renal tumors  $\leq$  4 cm. In some cases, tumors up to 7 cm located peripherally within the kidney can be reliably removed with partial nephrectomy. The key to sucreconstruction were the parameters evaluated for selecting cases for partial nephrectomy. 3-D MRI was accurate in predicting each of these parameters upon correlation with intraoperative and pathologic findings.

#### **Prostate Cancer**

Dr. Herbert Lepor moderated the session on prostate cancer. The faculty included Drs. Michael Brawer, MD (Northwest Prostate Institute), William

The key to success with partial nephrectomy in larger lesions is the ability to achieve a 1- to 2-cm tumor-free margin.

cess with partial nephrectomy in larger lesions is the ability to achieve a 1- to 2-cm tumor-free margin. The limitation to achieving this margin is major injury to the collecting system or the requirement for major venous reconstruction. Based on the relationship of the tumor to the hilar vessels noted in 3-D MRI, one may elect to clamp the renal artery. If the calyces represents the only site of entering, then direct closure rarely results in fistula. However, in cases requiring the opening of multiple calyces, infundibuli, or the renal pelvis, the risk of fistula is greater, and a radical nephrectomy is advised. Dr. Taneja has utilized the 3-D MRI, therefore, to select patients for partial nephrectomy based on these parameters. Another advantage of the 3-D MRI is the ability to detect lesions up to .6 mm in size. Because the 3-D MRI incorporates an MR angiographic phase, the relationship of the vessels to the tumor can be defined.

Dr. Taneja reviewed a series of 30 consecutive renal tumors presenting for surgery that were preoperatively examined using 3-D MRI. The absence of venous invasion, collecting system invasion, multifocality, and the likely necessity for major collecting system

Fair, MD (Cornell University), Edward Messing, MD (University of Rochester Medical Center), and Mitchell Steiner, MD (University of Tennessee).

#### **Tumor Markers**

Dr. Brawer provided an update on prostate serum markers. Dr. Brawer was one of the pioneers who popularized using prostate-specific antigen (PSA) for the screening of prostate cancer. In his early studies, approximately 30% of men with an elevated PSA were found to have prostate cancer. Dr. Brawer discussed several strategies for enhancing the specificity of PSA screening, which included PSA density, PSA velocity,

must be obtained. Recently, the Bayer Corporation has developed a specific PSA assay directed against complex PSA. A prospective screening study is presently underway that will define the clinical utility of complex PSA as a means to improve the assay's specificity.

Dr. Brawer discussed the role of human glandular kallikrein-2 (HK2) for improving the specificity of PSA screening. The HK2 protein has significant homology to PSA. It has been proposed that HK2 measurements in combination with measurement of free and total PSA can improve on the sensitivity and specificity of cancer detection and avoid unnecessary biopsies, especially in men with PSAs between 2.5 and 4.0 ng/dL. Studies are required to confirm these encouraging preliminary studies.

### Chemoprevention

Dr. Steiner discussed chemoprevention in prostate cancer. Dr. Steiner proposed that there are environmental factors that activate prostatic intraepithelial neoplasia (PIN) to clinical prostate cancer. He also considers PIN to be a clinical entity. Dr. Steiner proposed that the eradication of PIN would represent a chemopreventative strategy. Dr. Steiner presented evidence that estrogens are involved in the development of both

Preliminary data was presented suggesting that drugs with anti-estrogenic properties can eradicate prostatic intraepithelial neoplasia.

age-specific PSA reference ranges, and PSA molecular forms. The strategy of greatest clinical utility appears to be the assay for free and total PSA. In general, men with a lower percent of free PSAs have a greater chance of harboring prostate cancer. One of the primary disadvantages of free/total PSA ratios is that two separate assays benign prostatic hyperplasia (BPH) and prostate cancer. He also presented preliminary data suggesting that drugs with anti-estrogenic properties can eradicate PIN. If PIN is truly a premalignant disease, then preventing the development of PIN to cancer would have significant clinical utility, providing that cancer does not already exist at the time treatment is initiated.

Nutritional Aspects of Prostate Cancer Dr. Fair presented a discussion on the nutritional aspects of prostate cancer. He presented data showing that agespecific prevalence of histologic cancer is comparable between the United States and Japan. The fact that there was a dramatic difference in the prevalence of clinical prostate cancer in prostate cancer progression is unclear. The preponderance of the data from studies of selenium shows little advantage.

#### Interstitial Seed Implantation

Dr. Brawer discussed the technique of interstitial seed implantation and reviewed the results from the Northwest Prostate Institute. The objective of brachytherapy is to more precisely deliver the ionizing radiation

70%. In Dr. Brawer's opinion, modern prostate brachytherapy is a minimally invasive procedure that offers a viable alternative to surgery and conventional external beam radiation with excellent reported results for the treatment of clinically localized prostate cancer.

# Blood Management for Radical Prostatectomy

Dr. Lepor reviewed his experience with recombinant erythropoietin as a means to reduce transfusion requirements in men undergoing radical prostatectomy. The surgeon's interest in utilizing recombinant erythropoietin is based on individual transfusion requirements and patients' perception of the risk of transfusion.

Autologous blood donation is the most commonly used strategy for decreasing exposure to allogeneic blood following radical prostatectomy. Autologous blood donation creates an iatrogenic anemia, which results in the endogenous production of erythropoietin. The objective of preoperative erythropoietin administration is to increase red cell mass without the inconvenience of blood donation and the requirement for anemia.

Dr. Lepor's initial experience using a conservative regimen of erythropoietin demonstrated comparable effectiveness to autologous blood

The fact that there was a dramatic difference in the prevalence of clinical prostate cancer in the United States and Japan suggests a role for environmental factors in progression of prostate cancer.

in the United States and Japan suggests a role for environmental factors in progression of prostate cancer. Therefore, treatment that prevents progression of cancer may be of great interest. He also proposed that a goal for the treatment for prostate cancer may be control rather than cure.

Dr. Fair discussed several factors that may be involved in the progression of prostate cancer, including dietary fat, soybean products, vitamin A (carotenoids), vitamin E (tocopherols), and selenium. Epidemiological studies demonstrate that prostate cancer risk increases proportionally to the amount of fat and red meat in the diet. Studies performed by Dr. Fair have shown that the amount of fat in the diet regulates the growth of cancer cells inoculated into athymic mice. Altering dietary fat has also been shown to lower serum PSA levels in men with prostate cancer. All of these epidemiological experimental factors suggest that fat may be involved in the progression of prostate cancer. The very significant regional difference in clinical prostate cancer may also be related to the proportion of soy in the diet. Soy contains isoflavenoids. The effect of selenium to the prostate, thereby minimizing complications. In essence, modern brachytherapy is truly conformal. The procedure is done as an outpatient setting, and men return to daily activities within a day or two. Most implants utilize iodine-125 or palladium-103 (permanent implant). A few centers use the isotope iridium-192, which is temporarily implanted. The iodine-125 and palladium-103 seeds are permanent, because they employ low energy sources and have a relatively short half-life. The primary complications associated with brachytherapy include irritative and voiding symptoms, which, in most

A recent dose comparison study demonstrated that 300 IU of erythropoietin administered on preoperative days 14 and 7 is as effective as the previously used 600 IU.

cases, resolve within a few months. Urinary retention may occur, requiring catheterization. Incontinence rarely occurs unless men have undergone a prior transurethral prostatectomy (TURP), or require a TURP because of refractory retention. Disease-free survival at 12 years is approximately

donation. A subsequent study of a more aggressive preoperative dosing regimen of erythropoietin demonstrated greater effectiveness without any significant side effects. In a consecutive series of 283 men receiving erythropoietin, only one individual developed a cardiovascular compli-

Table 1 The Continence Index		
Parameter	Clinical Assessment	Points Assigned
1. Volume of bladder distention at which urine leaks around catheter	120 cc or more	3
	80 cc	2
	40 cc	1
	None	0
2. Continence while supine during the	Total continence	3
60 seconds immediately following	Minimal incontinence	2
catheter removal	Moderate incontinence	1
	Total incontinence	0
3. Continence while changing from supine	Total continence	3
to sitting position	Minimal incontinence	2
	Moderate incontinence	1
	Total incontinence	0
4. Continence while changing from sitting	Total continence	3
to standing position	Minimal incontinence	2
	Moderate incontinence	1
	Total incontinence	0
5. Ability to stop and start the urinary stream	Excellent	6
	Satisfactory	3
	Poor	0
Continence Score (0–18)	= Sum of assigned points	

cation. There were no adverse events attributed to erythropoietin. The mean increase in hematocrit was 2.8 units, which is equivalent to a unit of packed red blood cells. One of the disadvantages of administering 600 IU/kg 14 and 7 days preoperatively is the high cost. A recent dose comparison study demonstrated that 300 IU of erythropoietin administered on preoperative days 14 and 7 is as effective as the previously used 600 IU. Therefore, 300 IU administered 14 and 7 days preoperatively has a greater effect on increasing red cell volume, is less costly, and less cumbersome than autologous blood donation.

In summary, for those surgeons who feel it is prudent to decrease the risk of allogeneic blood exposure in radical prostatectomy, erythropoietin should represent the preoperative blood management strategy of choice.

Surgical Technique for Anatomic Radical Retropubic Prostatectomy Dr. Lepor presented several pearls related to radical prostatectomy. Dr. Lepor is editing a Urologic Clinics of North America, entitled Radical Prostatectomy, which will be published in the Summer of 2001. The technique that he presented at the meeting will be published in this upcoming volume.

# Incontinence Following Radical Prostatectomy

Dr. Lepor briefly discussed the mechanism of urinary incontinence. At the present time, there are no clinical characteristics or urodynamic parameters that predict who is at risk for developing incontinence. Fortunately, in the hands of experienced surgeons, the incidence of urinary incontinence is quite small.

The final continence status is typically achieved within 12 months of radical prostatectomy. It is conceivable that intervention, such as biofeedback, may facilitate the return of urinary continence. Dr. Lepor discussed a continence index that he developed that is a reliable predictor of the time to achieve urinary continence. The continence index is presented in Table 1. In Dr. Lepor's series, at 3 months following radical prostatectomy, 84% of men wore no pads or other than simply PSA elevation. At a median of 7.1 years follow-up, a significantly greater number of men in the delayed treatment arm died of their disease. Dr. Messing emphasized that this cohort of men represents minimal metastatic disease and discouraged extrapolating this data to all men with advanced prostate cancer.

Dr. Messing recognized that the

Biking provides tremendous cardiovascular benefit for the short-distance rider (15 to 20 minutes/day) with little to no risk of erectile dysfunction.

1 small pad over a 24-hour period, and 94% experienced no or slight bother due to their incontinence. The continence score predicted those men who experienced early return of continence. Dr. Lepor utilizes this continence index to select men for immediate biofeedback. Men who have a continence score ≤14 begin a regimen of biofeedback within 2 weeks of the catheter removal. This index has also shown to predict final continence status.

#### Androgen Deprivation

Dr. Messing presented his provocative study regarding the timing of androgen deprivation therapy for men with stage D<sub>1</sub> prostate cancer. The clinical utility of early hormonal intervention in prostate cancer is highly controversial. Although it is universally accepted that hormonal therapy is palliative, the value of early intervention on survival is controversial. In a study reported by Messing and associates, 98 men who underwent radical prostatectomy for clinically localized disease who were found to have nodal metastasis were randomized either to receive immediate hormonal monotherapy or to have treatment withheld until objective occurrence of disease progression

study included small numbers of patients and that the delayed treatment group behaved less well than other delayed interventions reported in the literature. Nevertheless, the randomized and prospective nature of the present study cannot be denied.

### **Erectile Dysfunction**

The session on erectile dysfunction (ED) was moderated by Andrew McCullough, Assistant Professor of Urology at NYU School of Medicine. The invited faculty included Irwin Goldstein, MD (Boston University) and Charles McCorkel, past president of Transportation Alternatives, a consumer action organization in New York City. Mr. McCorkle was an engineer by training and owns a bicycle store in New York City. The topics covered were new treatment options in ED, female sexual dysfunction, revascularization surgery, and the biking and erectile dysfunction controversy.

# Medical Treatment of Erectile Dysfunction

The first topic covered was a review of the medical treatment of ED. The first two years' experience with Sildenafil (Viagra) were reviewed, including post-marketing data on efficacy and safety. A recent study from the University of Pennsylvania on the safety of sildenafil in men with coronary artery disease, underscored the safety of sildenafil in men even with compromised coronary arteries, a group at highest risk for myocardial infarctions with sexual function.

This year, the centrally acting erectogenic drug, apomorphine was withdrawn by the sponsor before approval by the U.S. Food and Drug Administration (FDA). Concern about safety at high doses was the basis for this decision by an FDA review panel. Nonetheless, apomorphine has shown efficacy in mild to moderate ED in doses that cause no significant adverse events. It is anticipated that it will be approved and launched in Europe in early 2001.

The two new promising phosphodiesterase (PDE) inhibitors were reviewed, vardenafil and cialis, Both drugs demonstrate improved specificity for the PDE-5 over the PDE-6 inhibitors. Efficacy of these drugs is comparable to Viagra. Direct comparisons to sildenafil were not possible. because no head-to-head trials have been performed. It remains to be seen whether a safety profile or the side effect profile are significantly different from sildenafil.

#### Female Sexual Dysfunction

Dr. Goldstein gave an outstanding lecture on the new theories in the treatment of female sexual dysfunction. After a disappointing experience with sildenafil and female sexual dysfunction, attention has been more focused on endocrinologic abnormalities. Dr. Goldstein's laboratory has identified a subset of women who have a deficiency of dihydroepiandrosterone (DHEA). Replacement of this hormone in postmenopausal women with adrenal lyase deficiency seems to be beneficial in re-establishment of both libido and sexual function. Further clinical trials are needed to substantiate the benefit of DHEA supplementation.

## Bicycle Riding and Erectile Dysfunction

The final discussion, on bicycle riding and erectile dysfunction, provided a lively debate between biking supporters and Dr. Goldstein. Dr. Goldstein is well known for his belief that bicycle riding is detrimental to male sexual health through compression damage of the common penile arteries. Charlie McKorkle presented a viewpoint that biking provides a low impact, aerobic activity that offers cardiovascular benefits, weight

control, a decrease in osteoporosis, and an increased sense of well-being. In fact, bicycle ridership has decreased 50% since the ABC "20/20" program warning about the possible causal relationship between bicycle riding and ED. Unfortunately, many of the men have not substituted an alternative form of exercise.

Mr. McCorkel reviewed existing data on the association between biking and erectile dysfunction. Much of the data is anecdotal and poorly controlled and none is published in peer-reviewed journals. Though the data is frequently quoted as demonstrating the detrimental impact of biking versus running on erectile function, the impotence rate in bikers is clearly an order of magnitude lower than an age-matched cohort of the general population.

The overall conclusion was that biking provides tremendous cardiovascular benefit for the short-distance rider (15 to 20 minutes/day) with little to no risk of erectile dysfunction. Proper equipment, training, and technique are important to avoid injury for longer distance bike riders. Both Dr. Goldstein and Mr. McKorkle agreed that a more collaborative spirit between the biking industry and the medical community to truly define the risk of ED from biking would be beneficial to everyone.